# (19) World Intellectual Property Organization International Bureau



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## (43) International Publication Date 2 December 2004 (02.12.2004)

**PCT** 

# (10) International Publication Number WO 2004/104178 A3

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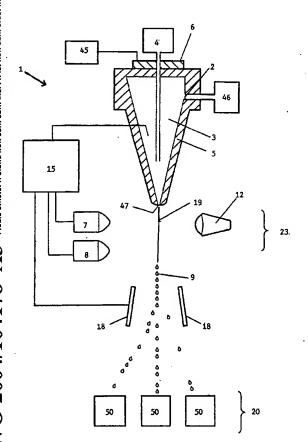
15 May 2003 (15.05.2003) US

- (71) Applicant (for all designated States except US): XY, INC. [US/US]; 1108 North Lemay Avenue, Fort Collins, CO 80524 (US).
- (72) Inventors; and
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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[Continued on next page]

#### (54) Title: EFFICIENT HAPLOID CELL SORTING FOR FLOW CYTOMETER SYSTEMS



(57) Abstract: A flow cytometry system (1) for sorting haploid cells, specifically irradiatable sperm cells, with an intermittingly punctuated radiation emitter (56). Embodiments include a beam manipulator (21) and even split radiation beams directed to multiple nozzles (5). Differentiation of sperm characteristics with increased resolution may efficiently allow differentiated sperm cells to be separated higher speeds and even into subpopulations having higher purity.

WO 2004/104178 A3 ||||||||||

## WO 2004/104178 A3



SI, SK, TR), OAPI (BF, BJ, CF, CG, CI; CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the international search report: 26 January 2006

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

International application No.

A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : G0 1N 33/00  US CL : 435/2; 422/73; 436/63  According to International Patent Classification (IPC) or to both national classification and IPC				
	DS SEARCHED	LIONAL CIASSIL	ication and IFC	
Minimum do	ocumentation searched (classification system followed 35/2; 422/73; 436/63	by classificat	tion symbols)	
Documentati	on searched other than minimum documentation to the	extent that	such documents are included in	n the fields searched
Electronic de EAST	ta base consulted during the international search (nam	e of data bas	se and, where practicable, sear	ch terms used)
C. DOC	UMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where a	ppropriate, o	of the relevant passages	Relevant to claim No.
A	US 6,149,867 A (SEIDEL et al.) 21 November 2000			1-230
A	US 4,559,309 A (EVENSON et al.) 17 December 19	85 (17.12.19	985), see entire document.	1-230
. English	documents are listed in the continuation of Box C.		See patent family annex.	
	pecial categories of cited documents:		later document published after the interns	stional filing data or migritu data
"A" document particular	defining the general state of the art which is not considered to be of relevance	"X"	and not in conflict with the application by principle or theory underlying the inventi document of particular relevance; the cla	nt cited to understand the con inned invention cannot be
"L" document establish	plication or patent published on or after the international filing date twhich may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"Y"	considered novel or cannot be considered when the document is taken alone document of particular relevance; the cla	imed invention cannot be
specified) "O" document	referring to an oral disclosure, use, exhibition or other means		considered to involve an invantive step v with one or more other such documents, : to a person skilled in the art	
"P" document	published prior to the international filing date but later than the		document member of the same patent far	nily
Date of the actual completion of the international search  Date of mailing of the international search report				
11 050 000				
19 November 2005 (19.11.2005)				
Ma Cor P.O	ailing address of the ISA/US il Stop PCT, Atta: ISA/US umissioner for Patents . Box 1450	Leon Eank	officer BNN GV	
Ala	xandria, Virginia 22313-1450	Telephone	No. (571) 272-1600	·
Facsimile No. (571) 273-3201				

International application No.

Box No. II	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)		
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:			
1.	Claims Nos.: 231 because they relate to subject matter not required to be searched by this Authority, namely: The claim reads on a human being.		
2.	Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:		
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Box No. III	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)		
This Internat	ional Searching Authority found multiple inventions in this international application, as follows:		
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ı. 🗌	As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.		
2.	As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.		
3.	As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:		
4.	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:		
Remark on			
	payment of a protest fee.  The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.		
	No protest accompanied the payment of additional search fees.		

#### PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY	
To: NICOLE A. RESSUE SANTANGELO LAW OFFICES, P.C. 125 SOUTH HOWES, THIRD FLOOR FORT COLLINS, CO 80521	PCT  NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION  (PCT Rule 44.1)
·	Date of mailing (day/monsh/year) 05 DFC 2005
Applicant's or agent's file reference XY-PULSE-PCT	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US04/15457	International filing date (day/month/year) 15 May 2004 (15.05.2004)
Applicant XY, INC.	
the applicant is hereby notified that the international search have been established and are transmitted herewith.  Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claimage of the search report.  When? The time limit for filing such amendments is a search report.  Where? Directly to the International Bureau of WIPO 1211 Geneva 20, Switzerland, Facsimile No.:  For more detailed instructions, see the notes on the account of the search report.  The applicant is hereby notified that no international scarce Article 17(2)(a) to that effect and the written opinion of the search report.	normally two months from the date of transmittal of the international 34 chemin des Colombettes (41-22) 338.82.70.  Example of the international Example of the international Example of the international searching Authority are transmitted herewith.  Example of the international searching Authority are transmitted herewith.  Example of the international searching of the international searching are transmitted herewith.
the protest together with the decision thereon has bee request to forward the texts of both the protest and the no decision has been made yet on the protest; the app	
4. Rensinders	maght will be housed as soon as a decision is made.
Shortly after the expiration of 18 months from the priority date Bureau. If the applicant wishes to avoid or postpone publication, claim, must reach the International Bureau as provided in Rules 9 preparations for international publication.	e, the international application will be published by the International a notice of withdrawal of the international application, or of the priority 0bis.1 and 90bis.3, respectively, before the completion of the technical the written opinion of the International Searching Authority to the
International Bureau. The International Bureau will send a coppreliminary examination report has been or is to be established, before the expiration of 30 months from the priority date.	y of such comments to all designated Offices unless an international These comments would also be made available to the public but not
examination must be filed if the applicant wishes to postpone the some Offices even later); otherwise, the applicant must, within 2 into the national phase before those designated Offices.	of some designated Offices, a demand for international preliminary entry into the national phase until 30 months from the priority date (in 0 months from the priority date, perform the prescribed acts for entry
In respect of other designated Offices, the time limit of 30 months	
See the Annex to Form PCT/IB/301 and, for details about the ap Volume II, National Chapters and the WIPO Internet site.	oplicable time limits, Office by Office, see the PCT Applicant's Guide,
Name and mailing address of the ISA/ US  Mail Stop PCT, Attn: ISA/US  Commissioner for Patents	Authorized officer Leon Lankfold

P.O. Box 1450
Alexandria; Virginia 22313-1450
Facsimile No. (571) 273-3201
Form PCT/ISA/220 (January 2004)

Telephone No. (571) 272-1600

(See notes on accompanying sheet)

## PATENT COOPERATION TREATY

# **PCT**

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference XY-PULSE-PCT	1	Form PCT/ISA/220
	1101111	re applicable, item 5 below.
International application No. PCI/US04/15457	International filing date (day/month/year) 15 May 2004 (15.05.2004)	(Earliest) Priority Date (day/month/year) 15 May 2003 (15.05.2003)
Applicant XY, INC.	·	
This international search report consists  It is also accompanies  1. Basis of the Report  a. With regard to the language, the international a translation of of a translation of the search claims were found.  2. Certain claims were found.  3. Unity of invention is lacking the text is approved as substituted.	of a total of sheets.  d by a copy of each prior art document cited in e international search was carried out on the ball application in the language in which it was fill the international application into	n this report.  sis of: ed, which is the language ch (Rules 12.3(a) and 23.1(b))
may, within one month from  6. With regard to the drawings,  a. the figure of the drawings to be  as suggested by the  as selected by this	ed, according to Rule 38.2(b), by this Authority in the date of mailing of this international searce published with the abstract is Figure No. 8	ch report, submit comments to this Authority.

Form PCT/ISA/210 (first sheet) (April 2005)

International application No.

Box No. II	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This internat	ional search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: 231 because they relate to subject matter not required to be searched by this Authority, namely. The claim reads on a human being.
2.	Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically.
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box No. III	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This Internat	onal Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on I	payment of a protest fee.
	The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
	No protest accompanied the payment of additional search fees.

International application No.

PCT/US04/15457

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A. CLAS	SIFICATION OF SUBJECT MATTER		
IPC(7)	: G01N 33/00		ļ
US CL : 435/2; 422/73; 436/63			
	International Patent Classification (IPC) or to both na	tional alassification and IDC	
		nonai classification and ii C	
B. FIELD	OS SEARCHED		
Minimum doc	cumentation searched (classification system followed	by classification symbols)	
	5/2; 422/73; 436/63		
0.5 43	312, 42213, 430103		
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Documentatio	on searched other than minimum documentation to the	extent that such documents are included in	i the news searched
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Electronic dat	ta base consulted during the international search (nam	e of data base and where practicable, sear	ch terms used)
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C. DOCU	JMENTS CONSIDERED TO BE RELEVANT	· · · · · · · · · · · · · · · · · · ·	2
Category *	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.
Α	US 6,149,867 A (SEIDEL et al.) 21 November 2000	(21.11.2000), see entire document.	1-230
	,	~ "	
Α	US 4,559,309 A (EVENSON et al.) 17 December 19	185 (17 12 1985) see entire document	1-230
^	03 4,339,309 A (E VENSON ET al.) 17 December 13	(17.12.1985), see entire document.	1-250
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Further	documents are listed in the continuation of Box C.	See patent family annex.	
• s	pecial categories of cited documents:	"T" later document published after the intern	
"A" document	defining the general state of the art which is not considered to be of	and not in conflict with the application be principle or theory underlying the invent	
	mievance	principle of aleasy animalying are involved	20
•	•	"X" document of particular relevance; the cla	imed invention cannot be
"E" earlierapj	plication or patent published on or after the international filing date	considered novel or cannot be considered	d to involve an inventive step
		when the document is taken alone	
	which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as	"Y" document of particular relevance; the cla	imed invention cannot be
specified)		considered to involve an inventive step	
		with one or more other such documents,	
"O" document	referring to an oral disclosure, use, exhibition or other means	to a person skilled in the art	
	published prior to the international filing date but later than the	"&" document member of the same patent fa	mily
priority a	ste claimed		·
Date of the a	ctual completion of the international search	Date of mailing of the international search	ch report
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19 November	r 2005 (19.11.2005)	\ _ 05 PAC 2009	
	ailing address of the ISA/US	Authorized officer	
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	il Stop PCT, Attn: ISA/US	Leon Banktord	(1)
1	mmissioner for Patents b. Box 1450	T   T   T   T   T   T   T   T   T   T	V
	n. 1900 Xandria, Virginia 22313-1450	Telephone No. (571) 272-1600	•
	o. (571) 273-3201	1 V	
I I GROSSITICIE INC	J. T. J. L. J. J. J. J. L.	1 -	

Form PCT/ISA/210 (second sheet) (April 2005)

#### PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING A	UTHORITY		
To: NICOLE A. RESSUE SANTANGELO LAW OFFICES, P.C. 125 SOUTH HOWES, THIRD FLOOR FORT COLLINS, CO 80521		PCT  WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY	
·			(PCT Rule 43bis.1)
		Date of mailing (day/month/year)	115 DFC 2009
Applicant's or agent's file reference		FOR FURTHER	ACTION
XY-PULSE-PCT			See paragraph 2 below
International application No.	International filing date	(day/month/year)	Priority date (day/month/year)
PCT/US04/15457	15 May 2004 (15.05.200		15 May 2003 (15.05.2003)
International Patent Classification (I	PC) or both national classificat	tion and IPC	•
IPC(7): G01N 33/00 and US Cl.: 435	5/2; 422/73; 436/63		
Applicant			•
XY, INC.		·—······	
This opinion contains indication	is relating to the following item	ns:	
Box No. I Basis of	of the opinion		
Box No. II Priorit	у		
Box No. III Non-ea	stablishment of opinion with re	egard to novelty, inves	ntive step and industrial applicability
Box No. IV Lack of	of unity of invention		
Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement			
Box No. VI Certain	n documents cited		
Box No. VII Certain	n defects in the international ap	oplication	
Box No. VIII Certain	n observations on the internation	onal application	
2. FURTHER ACTION			
If a demand for international p International Preliminary Exam	mining Authority ("IPEA") e o be the IPEA and the chosen	xcept that this does IPEA has notified the	be considered to be a written opinion of the not apply where the applicant chooses an at International Bureau under Rule 66.1bis(b) ered.
IPEA a written reply together, of Form PCT/ISA/220 or before	where appropriate, with amend e the expiration of 22 months fi	dments, before the ex	PEA, the applicant is invited to submit to the piration of 3 months from the date of mailing whichever expires later.
For further options, see Form P	CT/ISA/220.		
3. For further details, see notes to	Form PCT/ISA/220.		
Name and mailing address of the IS  Mail Stop PCT, Attn: ISA/US  Commissioner for Patents P.O. Box 1450  Alexandria, Virginia 22313-1	19 November	etion of this opinion 2005 (19.11.2005)	Leon Laukford Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (April 2005)

# WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

Box No. I Basis of this opinion	
•	
1. With regard to the language, this opinion has been established on the basis of:	
the international application in the language in which it was filed	
a translation of the international application into, which is the language of a translation furnished for the international search (Rules 12.3(a) and 23.1(b)).	purposes of
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary invention, this opinion has been established on the basis of:	to the claimed
a. type of material	
a sequence listing	
table(s) related to the sequence listing	
b. format of material	
on paper	
in electronic form	
c. time of filing/furnishing	
contained in the international application as filed.	
filed together with the international application in electronic form.	
furnished subsequently to this Authority for the purposes of search.	
1	
3. In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto or furnished, the required statements that the information in the subsequent or additional copies is identical application as filed or does not go beyond the application as filed, as appropriate, were furnished.	
4. Additional comments:	
·	
·	
·	
   Form PCT/ISA/237(Box No. I) (April 2005)	

# WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
the entire international application
claims Nos. 231
because:
the said international application, or the said claim Nos. 231 relate to the following subject matter which does not require an international search (specify):
The claim reads on a human being.
`\
the description, claims or drawings (indicate particular elements below) or said claims Nos are so unclear that no meaningful opinion could be formed (specify):
·
the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed (specify):
no international search report has been established for said claims Nos. 231
a meaningful opinion could not be formed without the sequence listing, the applicant did not, within the prescribed time limit:
furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).
a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.
the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
See Supplemental Box for further details.

# WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

Form PCT/ISA/237 (Box No. V) (April 2005)

International application No. PCT/US04/15457

Claims   NONE   NORE   NONE   NONE   NORE   NONE   NORE	itatement		•
Claims NONE NONE NO Claims 1-230 YE Claims NONE NONE NO Claims NONE NONE NO Claims NO Claims NONE NO Claims NONE NO Claims NONE NO CLAIMS NO	Novelty (N)	Claims 1-230	YE
Claims NONE NC  Industrial applicability (IA) Claims 1-230 YE  Claims NONE NC  Citations and explanations:  sims 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims methanalyzing sperm with a flow cytometer.  sims 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.			NC
Claims NONE NO YE  Industrial applicability (IA) Claims 1-230 YE  Claims NONE NO  Citations and explanations:  ims 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims method in the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.		Q1 :	V
Industrial applicability (IA)  Claims NONE  NO  Citations and explanations:  irms 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims meth analyzing sporm with a flow cytometer.  irms 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.	Inventive step (IS)		
Clatins NONE NO.  Citations and explanations:  hims 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims method analyzing sperm with a flow cytometer.  hims 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.	At	Charles 19919	
Citations and explanations:  sims 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims meth analyzing sperm with a flow cytometer.  sims 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.	Industrial applicability (IA)		YE
aims 1-230 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claims meth analyzing sperm with a flow cytometer.  Aims 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.		Claims NONE	NC
analyzing sperm with a flow cytometer.  hims 1-230 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed made or used in industry.	•	la 22(2).(2) because the prior art does not teach or fai	ely suggest the claims meth
made or used in industry.	nalyzing sperm with a flow cytometer.		
		le 33(4), and thus have industrial applicability because	the subject matter claimed
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